



Patent Docket P1761R1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| In re Application of Avi J. Ashkenazi et al. Serial No.: 09/603,866 Filed: June 26, 2000 For: Methods For Making Apo-2 Ligand Using Divalent Metal Ions | Group Art Unit: 1646 Examiner: E. Lazar-Wesley CERTIFICATE OF EXPRESS MAILING I hereby certify that this correspondence is being deposited with the United States Postal Service via Express Mail. Express Mail No. EJ563749876US in an envelope addressed to US Patent and Trademark Office, PO Box 2327 Arlington VA 22202. on November 27, 2001 <i>Diane L. Marschang</i> Diane L. Marschang |
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**RESPONSE TO RESTRICTION REQUIREMENT
AND
PRELIMINARY AMENDMENT**

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This paper is being filed in response to the Office Action mailed September 28, 2001. Entry of the following Amendment is respectfully requested prior to examination on the merits.

In the specification:

On page 7, in the paragraph on lines 7-22, the text has been amended as follows:

---While zinc binding sites have been shown to play structural roles in protein-protein interactions in certain proteins involving diverse interfaces [Feese et al., Proc. Natl. Acad. Sci., 91:3544-3548 (1994); Somers et al., Nature, 372:478-481 (1994); Raman et al., Cell, 95:939-950 (1998)], none of the previously structurally-characterized members of the TNF family (CD40 ligand, TNF-alpha, or TNF-beta) bind metals. The use of metal ions, such as zinc, in formulations of various hormones, such as human growth hormone (hGH), has been described in the literature. [See, e.g., WO 92/17200 published October 15, 1992). Zinc involvement in hGH binding to receptors was likewise described in